Main Participant Information Sheet & Consent Form

Interventional Study

Title	A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Event-Driven Study to Investigate the Effect of Orforglipron on the Incidence of Major Adverse Cardiovascular Events in Participants with Established Atherosclerotic Cardiovascular Disease and/or Chronic Kidney Disease
Short Title	ATTAIN-Outcomes
Protocol Number	J2A-MC-GZPW
Project Sponsor	Eli Lilly and Company
Principal Investigator	Dr. Cameron Booth
Location	33 Thorn Street, Ipswich, QLD 4305

Part 1 What does my participation involve?

1. Introduction

You are invited to take part in this research study. This is because you have established atherosclerotic cardiovascular disease and/or chronic kidney disease (hereinafter referred as heart related and/or kidney related disease). The research project is testing a potential new treatment for heart related and/or kidney related disease. The new treatment is called orforglipron.

This Participant Information Sheet and Consent Form tells you about the study. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want to take part in the study.

Please read this information carefully. Ask as many questions as possible about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or your local doctor.

Participation in this study is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care whether or not you take part.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

- Understand what you have read
- Consent to take part in the research project
- Consent to have the tests and treatments that are described
- Consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information Sheet and Consent Form to keep.

2. What is the purpose of this research?

Medications, drugs, and devices have to be approved for use by the Australian Federal Government Therapeutics Goods Administration (TGA). Orforglipron is not approved for the treatment of heart related and/or kidney related disease in Australia and therefore it is an experimental treatment in this study. This means that it must be tested to see if it is an effective treatment for heart related and/or kidney related disease

The purpose of this study is to learn more about orforglipron for the treatment of heart related and/or kidney related disease. The study aims to learn:

- Whether it can reduce the risk for major cardiovascular events.
- Whether it works better than a placebo (a placebo is an inactive or “pretend” study drug).
- What are the possible side effects.

The study is being conducted by Eli Lilly and Company and sponsored in Australia by Eli Lilly Australia Pty Ltd.

3. What does participation in this research involve?

If you agree to take part in this study and the study is suitable for you, you will get treatment as part of this study until the study doctor determines that you should not continue (for example, the study drug is no longer helping) or until the sponsor has collected all the information needed and the study ends.

Total participation is expected to be 5 years, but your participation may be shorter or longer depending on when the final visit for the study is determined, which your study doctor will discuss with you.

The study happens in periods. The activities may be a little different in each period, described in the sections below.

This study has 2 periods:

- **Screening Period:** Up to 2 weeks, 1 visit. You can have a maximum of 2 re-screening attempts.
- **Treatment Period:** Up to 5 years, but this may be shorter or longer depending on when the study ends

Throughout the Study

During the study, some of the activities might happen at the doctor's office, at your home, or at other places, depending on the study and local rules.
The study doctor will explain the study to you, including:

- which treatments you can still use,
- how the study will be done and what you'll need to do,
- and will answer any questions you have.

Screening Period

Before any study-related procedures are done, the study doctor will explain the study to you and you will have time to read this Participant Information Sheet and Consent Form and ask any questions you may have. The study staff will review this document with you and will help answer any questions you may have now and during the study. If you agree to participate in the study you will need to sign and date this consent form. You will be given a copy of the signed Participant Information Sheet and Consent Form to keep, and the original copy will be put in your medical record.

The first part of this study is the Screening Period. It lasts about 2 weeks depending on your personal health care situation. This period will help figure out whether you can continue to the next part of the study.

During this time, you will have some tests and activities, including:

- Medical and family history, including medicines, vitamins, and herbal supplements you take,
- Vital signs like heart rate and blood pressure,
- Height, weight, waist circumference, hip circumference, and physical examination,
- Blood draws and urine collection for laboratory tests,
- Electrocardiogram (ECG),
- you will be asked questions related to your conditions, and
- Other diagnostic tests like eye exams.

During this time, you can expect about 1 blood draw and about 1 ECGs, but you might need to have more. Serum pregnancy test will be performed during the screening.

You may be asked if you want to go through another round of screening procedures if you don't meet the screening criteria the first time. You can attempt another round of screening not earlier than 30 days from the date of the decision for each screen fail. The participants are allowed to have maximum two rescreening attempts. If you are eligible for the study at the end of the Screening Period, you will enter the Treatment Period. If the study doctor decides that you are not eligible to take part in this study, they will discuss other treatment options for your condition with you.

Treatment Period

You are expected to receive study treatment for up to 5 years, but this may be shorter or longer depending on when the study ends. Your study doctor will talk with you about your treatment duration and final visit. This is when you get either orforglipron or placebo to compare how well they work. We refer to these all together as "study drug." If you are eligible to stay in the study after you complete the Screening Period, and you decide to continue, you will enter the Treatment Period of the study.

You will be participating in a randomised controlled study. Sometimes we do not know which treatment is best for treating a condition. To find out we need to compare different treatments. We put people into groups and give each group a different treatment. The results are compared to see if one is better. To try to make sure the groups are the same, each participant is put into a group by chance (random). The likelihood that you will receive the drug being studied will depend on how the study is set up and is determined by chance. There is about a:

- 50% (1 in 2) chance of receiving orforglipron and
- 50% (1 in 2) chance of receiving placebo

You will be participating in a double-blind study. Neither you nor your study doctor will know which study drug you are getting. However, in certain circumstances your study doctor can find out which treatment you are receiving. A placebo is a medication with no active ingredients or a procedure without any medical benefit. It looks like the real thing but is not.

During this time:

- You will take study drug for about 5 years by mouth.
    - You may be asked to fast for some study visits.
    - Your dose will gradually be increased about every 4 weeks during the first 24 weeks until you get to the full regular dose.
    - The study drug can be taken with food or drink, must be swallowed whole, and cannot be crushed, chewed, or dissolved in liquid. You should try to take your dose at approximately the same time every day.
- You will have some tests/activities including:
    - Medical and family history, including medicines, vitamins, and herbal supplements you take
    - Vital signs like blood pressure and pulse rate,
    - Height, weight, waist circumference, hip circumference, and physical examination,
    - Blood draws and urine collection for laboratory tests,
    - ECG,
    - Questionnaires related to the study, and
    - Other diagnostic tests like eye exams.

During this time, you can expect about 14 blood draws and about 1 ECG, but you might need to have more. Serum pregnancy test will be performed during the screening while urine pregnancy test will be used during the duration of the study. If the urine pregnancy test is positive, additional pregnancy tests including serum test could be performed at investigator's discretion or required by local law or regulation. Ask the study doctor if you want to know more.

Each Treatment Period visit may be different in length depending on what tests will be done, but each visit is expected to take around 4 hours. Your study doctor will explain what you have to do and which tests you will have during the study.

This study has been designed to make sure the researchers interpret the results in a fair and appropriate way and avoids study doctors or participants jumping to conclusions. If you stop taking the study drug for any reason, the study doctor will still ask you to continue in follow-up.

Please read table 1 Study Procedures. This will give you information about what taking part in the study will mean to you, for example, does the visit requires fasting, how much blood will be taken and when tests and procedures will be performed.

Table 1. Study Procedures

Procedure	Screening	Dose-Escalation Treatment (Period II)							Maintenance Treatment (Period III)										
Visit (V)	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**EMV 24wk**	**EMV 48wk**	**PD TV**	**FV**
Weeks	*	**0**	**4**	**8**	**12**	**16**	**20**	**24**	**48**	**72**	**96**	**120**	**144**	**168**	**192**				
Visit Details	**O/F**	**O**	**O**	**O**	**O**	**O**	**O**	**O**	**O/F**	**D/L/T**	**O/F**	**D/L/T**	**O/F**	**D/L/T**	**O/F**	**D/L/T**	**O/F**	**O/F**	**O/F**
Informed consent	X																		
Check if the study is right for you	X	X																	
Questions	X																		
Safety Checks	X																		
Body Measurements	X	X	X	X	X	X	X	X	X		X		X		X		X	X	X
Vital Signs	X	X	X	X	X	X	X	X	X		X		X		X		X	X	X
Physical Checks	X	X	X	X	X	X	X	X	X	X	X		X		X	X	X	X	X
ECG	X	X	X	X	X	X	X	X	X	X	X		X		X	X	X		X
Eye Exam	X																		
Blood Sample (mL)	X (36)	X (32)			X (19.5)			X (42.5)	X (26.5)	X (10)	X (26.5)	X (10)	X (26.5)	X (10)	X (26.5)	X (10)	X (26.5)	X (26.5)	X (26.5)
Urine Sample	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Get Study Medicine		X																	
Take Study Medicine		X																	
Return Unused Study Medicine				X															

*-14 to 28 days prior to V2
F = fasting; O = office/on-site visit; D/L = dispensing/laboratory visit; T = telehealth optional;
FV = final visit; PDTV = permanent discontinuation of treatment visit; EMV = extended maintenance visit

What are the costs associated with joining the study?
You will receive the study drug, treatments, and procedures that are directly related to the study at no cost. Depending on how your healthcare expenses is paid for, you may have some personal expenses. The study staff can explain further.

If you spend money to be a part of this study, you may be able to get some or all of it back. You will only be given money back for expenses associated with study activities completed. The study staff will provide you and review more details around how reimbursement will be received.

If you decide to participate in this research project, the study doctor will inform your local doctor that you are participating and also of relevant clinical information disclosed in the conduct of the study.

4. What do I have to do?

If you decide to take part in this study, there are some rules you must follow. Some of the rules are listed below. There could be other rules that your study doctor will review with you. The study doctor will talk to you about any recommended or required lifestyle restrictions.

- You must follow the study procedures and go to all the study visits. Please inform the study doctor if you will not be able to attend a visit.
- You must follow all instructions given to you while you are taking part in this study. If you do not, you may no longer be able to take part in the study. If you are unsure about what you are supposed to do, ask your study doctor.
- You must report any changes to your well-being, including any side effects, to the study doctor.
- You must tell the study staff about any other medication you are taking or if you have any changes to your medications during the study. Tell the study doctor before you start a new medication.
- You are not allowed to take part in any other research study with an investigational product while you are in this research study.
- You must use and/or return the study drug during the study as instructed by the study doctor and study staff.

Below are the lifestyle changes that you may need to make if you participate in this study. Your study doctor will explain the lifestyle and medication changes you need to follow based on your situation.

Medication and Vitamins

- You may not be able to take your usual medications or supplements, and you may need to make some changes to your daily routine.
- You might need to take new medications to manage side effects or as part of the study. These new medications could have risks and might interact with the study drug(s).
- If you decide to take any new medications or supplements while in the study, make sure to talk to your study doctor first.

Meals and Diet

- You may need to avoid food and drinks before certain visits. The study doctor will remind you if this is the case.

- You may need to take the study drug with a meal or a certain amount of time before or after a meal.
- You are encouraged to follow a heart-healthy diet with more fruits, vegetables, whole grains, and low-fat dairy.

Caffeine, Alcohol, and Tobacco

- You should avoid the use of tobacco and limit the use of alcohol.

Other Lifestyle Restrictions

- You are encouraged to do at least 150 minutes of moderate exercise or 75 minutes of intense exercise each week, and to include muscle-strengthening activities on 2 or more days.
- You should not donate blood, semen, ova, organs, bone marrow, and other tissue during the study and for 14 weeks after your last dose of study drug.

The study doctor or a member of the study staff has discussed with you the requirements for participation in this research project. It is important that you are open and honest with the doctor and staff about your health history. You cannot take part in this research project if you do not meet all qualifications.

5. Other relevant information about the study

Up to 7140 participants will be taking part worldwide in this study. Up to 90 participants will be taking part in this study in Australia.

6. Do I have to take part in this study?

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage.

If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with Life Clinical Research.

7. What are the alternatives to participation?

You do not have to take part in this study get treatment for your condition. There are other treatment choices for your condition which may include:

- Different medicines to treat heart related and/or kidney related disease
- Non-medicine treatments for heart related and/or kidney related disease
- Choosing not to have any treatment

The study doctor can review your treatment options, how your condition is usually treated outside the study, and explain the possible benefits and risks, before you decide whether or not to take part in this study. You can also discuss the options with your local doctor.

8. What are the possible benefits of taking part?

No matter what treatment you receive as part of the study, you may not receive any medical benefits. This means that your heart related and/or kidney related disease may not improve or may get worse.

You will be given close attention from the study staff during the time you are involved in the study. You may get information about your health from physical examinations and medical tests done in this study.

If the results of this study are favourable and lead to approval of orforglipron in humans, there may be benefits for people with heart related and/or kidney related disease in the future.

There will be no clear benefit to you from your participation in this study.

9. What are the possible risks and disadvantages of taking part?

Participating in a clinical study:

- may require you to make lifestyle and medication changes, and
- could expose you to unknown risks
- could expose an unborn baby you are carrying or a baby you are breastfeeding to unknown risks

Medical treatments often cause side effects. You may have none, some or all of the effects listed below and they may be mild, moderate or severe. If you have any of these side effects or are worried about them, talk with your study doctor. Your study doctor will also be looking out for side effects.

There may be side effects that the researchers do not expect or do not know about and that may be serious. **If you have unexpected or troubling symptoms while you are in the study, contact your study doctor and, if you feel it is necessary, seek emergency medical care.** Many side effects go away shortly after treatment ends. However, sometimes side effects can be serious, long lasting, or permanent. If a severe side effect or reaction occurs, your study doctor may need to stop your treatment. Your study doctor will discuss the best way of managing any side effects with you. Below are the known risks for you to consider if you participate in this study.

Allergic reactions

- Serious allergic reactions have been reported in participants who have taken drugs like orforglipron. This has not been reported for orforglipron.
- Less commonly, a more serious reaction may occur that can sometimes be life-threatening.
- You will be watched for signs of allergic reactions during the study. If you develop symptoms of an allergic reaction during or after an administration of orforglipron and if these symptoms are not normal for you, you should seek immediate medical attention and ask your study doctor about whether you should continue with the treatment.

Allergic reaction is always possible with a drug especially if you have not taken it before. Serious allergic reactions (anaphylaxis) that can be life-threatening may occur. Some things that happen during an allergic reaction to any type of medication are:

- Rash
- Joint pain
- Having a hard time breathing

- Wheezing when you breathe
- Sudden drop in blood pressure
- Swelling around the mouth, throat, or eyes
- Fast pulse
- Sweating

<u>If you experience these symptoms, you should seek urgent medical help at an Emergency Department or call an ambulance.</u>

<u>Driving and Using Machines</u>

It is possible that orforglipron may affect your ability to drive or use machines. If you have signs of allergic reaction such as chills, fever or dizziness during treatment, don't drive or use machines until your symptoms go away.

Risks for drugs in the study

Below are the known risks for the study drug being tested. You may experience some, all, or none of the side effects listed below.

942 people have taken orforglipron in the completed clinical trials. Of these,

- 268 were healthy adults
- 380 were adults with type 2 diabetes mellitus, and
- 294 were adults with obesity or overweight.

Risks for All Studies

Table 2 shows the side effects people had when taking orforglipron.

Table 2. Very Common and Common Side Effects of the Study Drug

Very Common (greater than or equal to 10%)	Common (greater than or equal to 1% but less than 10%)
Feeling sick to the stomach	Bloating
Throwing up	Indigestion
Hard or infrequent stools	Heartburn
Watery, loose, or frequent stools	Dizziness
	Increases in heart rate to above normal limits (more than 100 beats per minute)

Some people who have taken medicines that work like orforglipron have reported the side effects below. Some of these side effects have been reported with orforglipron, as stated below:

Stomach- or gut-related effects

- Most common side effects seen with drugs that are like orforglipron include stomach and gut effects. These effects may include decreased food movement in the stomach, feeling sick, loose or watery stools, hard or infrequent stools, and throwing up.
- Serious side effects involving the stomach or gut have been observed with orforglipron and drugs that are like orforglipron.

Worsening kidney function

- Worsening kidney function has been reported as a serious side effect in people who have taken drugs that are like orforglipron.
- Worsening kidney function may occur if you become severely dehydrated (lose too much water) from throwing up, and/or having watery, loose, or frequent stools. Dehydration is a risk factor and may lead to acute kidney failure.
- Worsening of kidney function has not been reported for orforglipron.
- Please notify your study doctor if you have symptoms of dehydration. You may need to go to the hospital for treatment. The treatment may include having fluids given to you through the blood vessels in your arm.

Low blood sugar

- Low blood sugar has been reported as a side effect in people who have taken drugs that are like orforglipron. Low blood sugar may occur if you have type 2 diabetes mellitus and are taking additional blood-sugar-lowering medications. If it is very low, it can lead to seizures, loss of consciousness, or coma, which may be life-threatening.
- One participant in completed studies had severely low blood sugar level after taking orforglipron and was hospitalized.
- If you have type 2 diabetes mellitus, your blood sugar level will be checked regularly during the study.

Inflammation of the pancreas

- Pancreatitis is an inflammation (swelling and pain) of the pancreas, an organ in your belly that helps with digestion and produces insulin.
- One person had a confirmed case of acute pancreatitis after taking orforglipron.
- If severe, this can be life-threatening. You may be asked to return to the study site to be evaluated, which may include blood tests and x-rays.

Pancreatic cancer

- Participants with type 2 diabetes mellitus or with obesity have been shown to have an increased risk of pancreatic cancer.
- Pancreatic cancer has not been reported in study participants who have taken orforglipron.

Increased heart rate

- Increased heart rate has been reported as a side effect in people who have taken drugs like orforglipron.
- Increase in heart rate has been observed in study participants with orforglipron.
- The electrical activity of your heart rate (including heart rate and rhythm) will be closely watched during this study.

Thyroid cancer

- A rare form of thyroid cancer (medullary thyroid cancer) has been reported in animals who have been given drugs that are like orforglipron. This has not been reported in participants who have taken orforglipron.
- If you or anybody in your family (blood relatives only) had this rare form of thyroid cancer (medullary thyroid cancer) or a cancer disease called “multiple endocrine neoplasia syndrome type 2,” please tell the study doctor, because you should not receive orforglipron.

- If you are participating in a study with orforglipron, your calcitonin levels will be measured. Calcitonin is a hormone that helps control how the body uses calcium. It is made by some cells in the thyroid that can develop into medullary thyroid cancer.
- If medullary thyroid cancer is suspected or if you have someone in your family with medullary thyroid cancer, blood tests of calcitonin levels can help look for medullary thyroid cancer.

Liver and gallbladder disease

- Increases in liver blood tests have been reported as a side effect in people who have taken drugs like orforglipron. Increases in liver blood tests have been reported in participants receiving orforglipron. Liver tests will be monitored and, if significant changes in these tests are observed, appropriate medical treatments will be instituted as needed.
- Gallbladder stones and disease have been observed with other drugs similar to orforglipron. This risk may be increased in people who have diabetes or obesity, and when rapid weight loss occurs.
- Gallbladder disease has been reported in participants receiving orforglipron. These events will be monitored and appropriately managed in clinical studies with orforglipron.
- Some gallbladder problems may need surgery.

Poor nutrition

- Poor nutrition has been reported in people who have taken drugs like orforglipron. No cases of poor nutrition have been reported for orforglipron.
- Poor nutrition may occur if you have experienced loss of appetite and you do not eat properly to ensure you are getting enough nutrients.
- Tell your doctor if you have very low food intake and would like help with nutrition.

Food or liquid getting into lungs

- Drugs like orforglipron cause stomach to take too long to empty its contents. Some people taking medicines that work like orforglipron have had problems with food or liquid getting into the lungs when having a medical procedure (for example, surgery) that required medications to put them to sleep or keep them from feeling pain.
- Tell your study doctor if you are scheduled to have a procedure that requires such medications.

Effects with other drugs

- Sometimes drugs that are like orforglipron may affect the way that other medicines work. In addition, other medicines may affect the way that orforglipron works. This means some medicines or orforglipron may not work as well and may pose safety risks or an increased chance of side effects if they are taken at the same time.
- You should tell the study doctor if you are taking any other medicines.

Risks for Participants with Type 2 Diabetes Mellitus

Orforglipron has been given to 380 adults with type 2 diabetes mellitus. The common and very common side effects that occurred are captured above. Additional common side effects they had were:

- belching

- passing gas
- headache
- stomach pain, and
- feeling tired.

Risks for Participants with Obesity or Overweight

Orforglipron has been given to 294 adults with obesity or overweight. The common and very common side effects that occurred are captured above. Additional very common side effects they had were:

- belching
- stomach pain, and
- feeling tired.

Safety Data from Animal Studies

Orforglipron has been given to animals. The information from animal studies may be useful to you in considering whether to participate in the study because similar effects could be observed in people. Important effects seen in animals are:

- mild and temporary changes in liver test results without causing any symptoms
- changes in heart rate
- throwing up
- loss of appetite, and
- weight loss.

No undesired effects on any body organs were seen in animal studies.

Important Symptoms for All Studies

It is important to notify the study doctor right away if you have any of the problems below, because they could indicate a serious problem.

Call the Study Doctor Right Away if you Have…	Because it may indicate…
For All Participants	
Severe feeling of sickness, pain in the stomach, frequent throwing up, and watery, loose, or frequent stools	Stomach- or gut-related effects
Thirsty, feeling dizzy (especially while standing), tired, weak, less water intake, dryness of the lips, eyes, mouth or skin, and dark yellow and strong-smelling pee	Symptoms of dehydration that may lead to worsening function of the kidneys
Low energy, hungry, confused, a pounding heart, sweating, shakiness, and headache	Low blood sugar
Severe stomach pain that is not normal for you or if you feel sick to the stomach with or without throwing up	Pancreatitis
Chest pain, pounding heart, or an irregular or "skipped" heartbeat	Increased heart rate
Fever, chills, joint pain, muscle pain, skin rash, sickness in the stomach, dizziness, headache, throat irritation, shortness of breath, low blood pressure, wheezing, and difficulty in breathing.	Allergic or hypersensitivity event
Pain in the upper stomach (abdomen), fever, yellowing of the skin or eyes (jaundice), and clay-colored stool	Liver and gallbladder disease

For Type 2 Diabetes Mellitus	
Not applicable	Not applicable
For Obesity or Overweight	
Not applicable	Not applicable
For Pediatric Participants	
Not applicable	Not applicable

Risks for study procedures

There might be some risks with the activities in this study. Most of the activities are regular medical procedures, and the risks are the same whether they are done in the study or outside of it. The study staff can answer any questions you have about what will happen in the study and the risks for you.

The following are risks associated with the activities in this study.

Blood Tests	You might feel a quick pinch when the needle goes in, and sometimes a bruise might form. After the procedure, you might feel dizzy or faint.
ECG	You might feel a bit of discomfort when the devices are placed on or removed from your skin. You might have mild skin irritation after the test.
Urinalysis	You may be asked to urinate or "pee" into a small cup in the privacy of a toilet area. There is usually no discomfort.

Reproductive Risks

There is no clinical study experience with orforglipron in pregnant or breastfeeding participants, and the potential effects of orforglipron use during pregnancy and breastfeeding are not known. Women of childbearing age can participate in orforglipron clinical studies as long as they use acceptable birth control methods. Because of this, it is important that research project participants are not pregnant or breast-feeding and do not become pregnant during the course of the research project. You must not participate in the research if you are pregnant or trying to become pregnant, or breast-feeding. If you are female and child-bearing is a possibility, you will be required to undergo a pregnancy test prior to commencing the research project. The study medicine should not be used during pregnancy as the effects of this medicine on an unborn child are not known

Both female and male participants must use highly effective contraception (birth control) during the course of the research project and for 2 weeks after receiving the last dose of study medication. There may be risks of interactions between the study medication and certain kinds of birth control. Your study doctor can discuss your specific risks in more detail. The study doctor will review with you whether you may need to use birth control, which methods of birth control are required, or any other restrictions needed while you are in the study. Some effective methods of birth control are listed below.

Highly effective methods of contraception include:

- Combined (oestrogen and progesterone containing) hormonal contraception by oral or intravaginal route or dermal patches
- Progestogen-only hormonal contraception associated with inhibition of ovulation given by oral route or by injections or implants
- Intrauterine device (IUD)
- Intrauterine hormone-releasing system (IUS)
- Bilateral tubal occlusion
- Vasectomised partner
- Complete sexual abstinence, where this is your usual and preferred lifestyle

For female participants: If you take birth control pills, you should also use another form of protection (e.g., a condom) or switch to a non-oral birth control method. Birth control should be used during the study and for 2 weeks after receiving the last dose of study medication. You should not donate ova/egg for 14 weeks after receiving the last dose of the study medication. Tell your doctor right away if you or your sexual partner(s) become pregnant or plan to breastfeed, as the study doctor may ask for more information about the pregnancy and health of the child. Your study doctor will withdraw you from the research project and advise on further medical attention should this be necessary. You must not continue in the research if you become pregnant.

For male participants: Birth control should be used during the study and for 2 weeks after receiving the last dose of study medication. You should not father a child or donate sperm during the study and for 14 weeks after receiving the last dose of study medication. Tell your doctor right away if you or your sexual partner(s) become pregnant or plan to breastfeed, as the study doctor may ask for more information about the pregnancy and health of the child. Your study doctor will advise on medical attention for your partner should this be necessary.

10. What will happen to my test samples?

Samples of your blood and urine will be collected from you during this study. Please see the information below to learn more about how your samples will be used and who will have access to them. The collection of these samples is required for you to participate in this study.

Type	Purpose	Length of time stored	Who may use it or see your data	Notes
Blood and Urine	To confirm that you can be in the study and monitor your health.	Until tests are done and confirmed	Only researchers in this study	You may be tested for hepatitis, HIV, or other diseases. If blood tests say you have one of these diseases, researchers will contact you. Certain results may be required to be shared to others based on local law.
Blood	To learn more about heart related and/or kidney related disease or how people respond to the study drug.	Up to 7 years after all participants have finished the study	Study researchers and others*	Biomarkers are substances in the body that can tell researchers about a condition. For example, cholesterol in the blood can be a biomarker for heart disease.
Blood	To learn how the study drug works for you or to help find out why people react to drugs differently.	Up to 7 years after all participants have finished the study	Study researchers and others*	DNA and RNA tell your body how cells should be built and work. Some of these instructions tell your body how to react to drugs. Your DNA will be used for additional research related to orforglipron or other cardiovascular diseases (CVD), kidney disease, liver disease, and other related diseases. This may involve the analysis of specific genes or genetic markers in your DNA to help better understand your condition or other relevant disease.

"Others" refers to a business partner or collaborator of the Sponsor who will be required to sign a written agreement to protect your samples and uses the samples as agreed to in this Participant Information Sheet/Consent Form.

Your samples will be assigned a unique identifying code, but not your name or other individually identifiable information. The study site will share your samples with the Sponsor only after they have been coded, therefore the data is not able to identify you.

All samples will be destroyed based on laboratory procedures, laws, regulations, or international laboratory standards.

Your biological samples

During the study, we may collect your blood and urine to monitor your health, evaluate how the study drug is working, and learn more about the study drug and your heart related and/or kidney related disease.

Neither you nor the study doctor will obtain the results of these tests. This type of testing is done to further our knowledge about how the study drug works and it will not produce the type of results that will have any useful meaning that would affect your health or treatment. Therefore, you will not be informed of the results of the tests.

The type of testing being done in this research project is not testing that would result in information about a participant's future health or risk of having children with a genetic disorder, or information that may be relevant to the health of family members who are not part of the trial.

The proposed blood tests include a screening test for HIV (also called the 'AIDS' virus) and Hepatitis. This is because the study doctors need to know if you could participate the study. You will receive information and counselling by the study doctor before the test. If a test shows you have HIV or Hepatitis, you will have follow-up counselling and medical advice. **If your test results are positive, the study doctors are required by law to notify government health authorities.** Signing the consent form means that you agree to have this testing; it will not be done without your consent.

11. What if new information arises during this study?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If any important new information is found during this research project that may affect you wanting to continue to be part of this research project, you will be told about it right away.

If you decide to withdraw, your study doctor will make arrangements for your regular health care to continue. If you decide to continue in the research project, you will be asked to sign an updated consent form. Also, on receiving new information, your study doctor might consider it to be in your best interests to withdraw you from the research project. If this happens, your study doctor will explain the reasons and arrange for your regular health care to continue.

12. Can I have other treatments during this study?

Whilst you are participating in this research project, you may not be able to take some or all of the medications or treatments you have been taking for your condition or for other reasons. It is important to tell your study doctor and the study staff about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments. You should also tell your study doctor about any changes to these during your participation in the research project. Your study doctor should also explain to you which treatments or medications need to be stopped for the time you are involved in the research project.

13. What if I withdraw from this study?

If you decide to withdraw from the study, please notify a member of the study team before you withdraw. This notice will allow that person or the study supervisor to discuss any health risks or special requirements linked to withdrawing.

If you do withdraw your consent during the study, the study doctor and relevant study staff will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected by the sponsor up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must tell them before you join the research project.

14. Could this study be stopped unexpectedly?

This study may be stopped unexpectedly for a variety of reasons. This could happen if the Sponsor or the study doctor learns new information about the safety of the study drug or the trial, if the study drug is shown not to be effective, if the study drug is shown to work and not need further testing, or for decisions made in the interests of the Sponsor or local regulatory/health authorities, or closes the study location.

The study doctor or the Sponsor may also remove you from the study or stop your study drug. This may be because of a bad reaction you experience, become pregnant, find out which treatment you are getting before the study ends, or because you did not follow the study plan or the instructions of the study staff. If you are taken off the study, you will no longer receive the study drug. If your study drug is stopped, your study doctor will closely monitor your overall health.

15. What happens when the research project ends?

Currently, orforglipron will not be provided after the end of the study. If your condition requires further treatment, your study doctor will help you decide what treatment is best for you after the end of the study. Your doctor will speak to you about your health care options. At the time that your participation in this study ends, an extension study testing orforglipron may be available for you to join. Your study doctor will tell you about this if the option becomes available for you.

When the study is over, a summary of the results will be made available. The study doctor can provide more details about when and where you can access the results. You may ask your study doctor to explain the results to you.

A description of this clinical trial will be available on https://www.ClinicalTrials.gov. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time. Requirements to join the trial and countries participating can be found on this website.

Information regarding this study can also be found at www.euclinicaltrials.eu/search-for-clinical-trials/ with the study number 2025-523123-22-00.

Study data collected as part of this research study may be published in study reports or medical journals, used for scientific presentations, and may also be shared with, or inspected by, health authorities worldwide. Information that identifies you or that reasonably could be used to identify you will not be included in such publications.

Part 2 How is the research project being conducted?

16. What will happen to information about me?

If you choose to participate in this study sponsored by Eli Lilly and Company ("Lilly"), the study doctor and study staff will collect certain personal information ("PI") about you. This data privacy section describes how your PI will be used and with whom it may be shared. It also describes your rights with respect to this information.

Your information

Your personal information (PI) is information that identifies you or could reasonably be used to identify you. There are different types of PI that can be collected as part of your participation in the study. Categories of PI that are collected include, your basic personal details (e.g., name, alias, birth year, email, etc.), health information (e.g. medical history, prescriptions, test results, etc.), and certain characteristics such as race and ethnicity.

Your PI will be used and shared for the purposes of conducting and overseeing this study as described in this document. Some of the uses include determining if you are eligible for this study, understanding your medical history, assessing your health and providing medical treatment during the study. The study doctor and study staff will collect the PI about you from your existing health records or directly from you, and store it in a study specific database only accessed by authorised individuals.

If you are not able to attend a planned study visit or maintain telephone contact, the study doctor or staff may try to contact you to check on your health status and to see if you have experienced a serious health event. The study doctor or staff may try to locate you and search your information by making contact with a family member, your family doctor, and hospitals and clinics that treat you. The study doctor or staff will try to contact you unless you withdraw consent of getting contacted further. Attempts to determine your health status may also be done by searching public records such as national registries or databases and voter records, if not prohibited by your local laws and regulations.

How is your personal information protected?

The study doctor and study staff will share information that does not directly identify you (e.g name, address and date of birth) with Lilly and representatives working on behalf of Lilly. The study doctor and study staff will assign a code number to your PI to protect your identity.

How is your coded information used and shared?

Lilly may use this coded data in the following ways:

- As part of this study;
- To meet global regulatory requirements and approvals;
- To publish its findings in study reports or scientific presentations;
- For further medical research projects, the specific details of which may not be fully known at present;
- For further examination by Lilly, its affiliates, and with business partners of the safety or efficacy and/or identification of new medical uses of any medical product or treatment included in the study;
- For further examination of the disease(s) or condition(s) that are the subject of the study to identify new learnings;
- To analyze how Lilly can improve its clinical research processes; and,
- To develop Artificial Intelligence and/or Machine Learning ("AI/ML") tools that will assist in further examination of the disease(s) or conditions that are the subject of the study.

Lilly may share this coded data for the purposes in this document with its affiliates, business partners, regulatory authorities in countries around the world, and ethics committee(s). Once shared, this data may fall under data protection laws in other countries that may be less protective than data protection laws in the country or region in which you are participating in this study, however, Lilly will continue to protect your coded data and use the data only for the purposes described in this document.

How long will your information be stored?

Records containing your PI will be retained at the study site for a period of up to 15 years after the end of the study. In addition, Lilly will retain the coded data for up to 5 years after marketing of the study drug has completed.

How do I agree to the use of my information for this study?

By signing this document, you agree to the collection, use, and disclosure of your PI as described in this document. If you do not provide your consent, it will not affect your current or future medical treatment, payment for your treatment, enrolment in or eligibility for benefits to which you are otherwise entitled. And, if you do not consent, you will not be able to participate in this study.

What are my rights related to my information that is collected, used, or shared during the study?

You have the right to withdraw your consent for the collection, use, and disclosure of your PI for this study at any time. If you decide to withdraw your consent, you cannot continue to participate in the study. PI collected prior to your withdrawal of consent must be maintained in the study records due to regulatory requirements. To meet regulations, Lilly, its affiliates, or its business partners may need to collect information about your health status after you withdraw from the study.

You may also have other legal rights related to your PI based on where you participate in the study. You may contact the study site staff listed in “Further information and who to contact” to understand your rights.

If you are not satisfied with the response or believe the Study Site or Lilly are not processing your PI in accordance with the law, you can file a complaint with the relevant regulatory authority (e.g., a Data Protection Authority such as the Office of the Australian Information Commissioner, or your applicable state-based equivalent.)

Sponsor request for confidentiality
The sponsor wants to keep the information in this document confidential. Please share it only if you need to decide whether to join or stay in the study, if you have questions about your rights, or when getting medical care from healthcare professionals.

17. Complaints and compensation

If the study plan is followed correctly, you follow the directions of the study doctor and staff and you are physically injured as a direct result of a study procedure or drug, you should contact your study doctor as soon as possible for assistance with arranging appropriate medical treatment. If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

There are two avenues that may be available to you for seeking compensation if you suffer an injury as a result of your participation in this study:

- The pharmaceutical industry has set up a compensation process, with which the Sponsor, Eli Lilly Australia Pty Ltd, of this research project has agreed to comply. Details of the process and conditions are set out in the *Medicines Australia Guidelines for Compensation for Injury Resulting from Participation in a Company-Sponsored Clinical Trial.* In accordance with these Guidelines, the sponsor will determine whether to pay compensation to you, and, if so, how much. A copy of the Guidelines is available to you from the research staff on request.

- You may be able to seek compensation through the courts.

18. Who is organising and funding the study?

This study is being conducted by Eli Lilly and Company, and sponsored in Australia by Eli Lilly Australia Lty Ltd.

Eli Lilly and Company may benefit financially from this study if, for example, the project assists Eli Lilly and Company to obtain approval for a new drug/device.

By taking part in this study you agree that samples of your blood or tissue (or data generated from analysis of these materials) may be provided to Eli Lilly and Company. Eli Lilly and Company may directly or indirectly benefit financially from your samples or from knowledge acquired through analysis of your samples.

You will not benefit financially from your involvement in this study even if, for example, your samples (or knowledge acquired from analysis of your samples) prove to be of commercial value to Eli Lilly and Company.
In addition, if knowledge acquired through this research leads to discoveries that are of commercial value to Eli Lilly and Company, the study doctors or their institutions, there will be no financial benefit to you or your family from these discoveries.

Life Clinical Research will receive a payment from Eli Lilly and Company for undertaking this research project.

No member of the research team will receive a personal financial benefit from your involvement in this study (other than their ordinary wages).

19. Who has reviewed this study?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of Monash Health.

This research project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2025 - incorporating all updates)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

20. Further information and who to contact

The person you may need to contact will depend on the nature of your query.
If you want any further information concerning this study or if you have any medical problems which may be related to your involvement in this study (for example, any side effects), you can contact the principal study doctor on 07 3180 8045 or any of the following people:

Clinical contact person

Name	Dr. Cameron Booth
Position	Principal Investigator and Cardiologist
Telephone	3180 8045
Email	cameron@LCR.Health

For matters relating to research project at the site at which you are participating, the details of the local site complaints person are:

Complaints contact person

Name	Paul Christensen
Position	Clinical Operations Director
Telephone	0417 108 585
Email	Paul@LCR.Health

If you have any questions, concerns or complaints about your rights as a participant in a research project, please contact:

Reviewing HREC approving this research project and HREC Executive Officer details

Reviewing HREC Name	Monash Health Human Research Ethics Committee
HREC Executive Officer	HREC Executive Officer
Telephone	(03) 9594 4611
Email	research@monashhealth.org

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Main Participant Consent Form

Title	A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Event-Driven Study to Investigate the Effect of Orforglipron on the Incidence of Major Adverse Cardiovascular Events in Participants with Established Atherosclerotic Cardiovascular Disease and/or Chronic Kidney Disease
Short Title	ATTAIN-Outcomes
Protocol Number	J2A-MC-GZPW
Project Sponsor	Eli Lilly and Company
Principal Investigator	Dr. Cameron Booth
Location	33 Thorn Street, Ipswich, QLD 4305

Consent Agreement

Joining the study is your decision. To agree to take part in this study, please sign and date below. Signing this consent page means that:

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand all of the information I have been given about this study.

I give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to **release information to Life Clinical Research** concerning my disease and treatment for the purposes of this project. I understand that such information will remain confidential.

I have had an opportunity to ask questions, all of my questions have been answered, and I have had time to think about the study.

I agree to be part of the study as described, and I understand that I can decide to withdraw from the study at any time without affecting my future health care.

I have given my free and informed consent to be part of this research study. I understand that I will be given a signed copy of this document to keep.

Declaration by Participant Who Have Read the Information

Name of Participant (please print) _____

Signature _____ **Date** (dd mmm yyyy) _____

For Participants Unable to Read the Information and Consent Form

See Note for Guidance on Good Clinical Practice CPMP/ICH/135/95 Section 4.8.9. A legally acceptable representative may be a witness*

Name of Witness to the Informed Consent Process (please print) _____

Signature _____ **Date** (dd mmm yyyy) _____

* Witness is not to be the Investigator, a member of the study team or their delegate. Witness must be 18 years or older.

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the study, its procedures and risks and I believe that the participant has understood that explanation.

Name of Study Doctor or Senior Researcher‡ (please print) _____

Signature _____ **Date** (dd mmm yyyy) _____

† A senior member of the research team must provide the explanation of, and information concerning, the study.

Note: All parties signing the consent section must date their own signature.

Main Form of Withdrawal of Participation

Title	A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Event-Driven Study to Investigate the Effect of Orforglipron on the Incidence of Major Adverse Cardiovascular Events in Participants with Established Atherosclerotic Cardiovascular Disease and/or Chronic Kidney Disease
Short Title	ATTAIN-Outcomes
Protocol Number	J2A-MC-GZPW
Project Sponsor	Eli Lilly and Company
Principal Investigator	Dr. Cameron Booth
Location	33 Thorn Street, Ipswich, QLD 4305

Declaration by Participant

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine treatment, my relationship with those treating me or my relationship with Life Clinical Research

Declaration by Participant Who Have Read the Information

Name of Participant (please print) _____

Signature _____ **Date** (dd mmm yyyy) _____

In the event that the participant's decision to withdraw is communicated verbally, the Study Doctor/Senior Researcher will need to provide a description of the circumstances below:

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the implications of withdrawal from the study and I believe that the participant has understood that explanation.

Name of Study Doctor or Senior Researcher‡ (please print) _____

Signature _____ **Date** (dd mmm yyyy) _____

† A senior member of the research team must provide the explanation of, and information concerning, the study.

Note: All parties signing the consent section must date their own signature.